

Conjugate Pneumococcal Vaccines: Need and Choice in India

Introduction

Streptococcus pneumoniae (pneumococcus) is a leading cause of bacterial pneumonia, meningitis and sepsis in children. Otitis media, sinusitis and bronchitis are more common, but less serious manifestations of this infection. *Streptococcus pneumoniae* causes 0.7-1 million deaths in children <5 years.⁽¹⁾ Among under five children pneumonia caused by pneumococcus accounts for more than 50% of all pneumonia cases world-wide.⁽²⁾ In the developed world, children aged <2 years and elderly people carry the major burden of disease.⁽³⁾ Rising antimicrobial resistance among *S. pneumoniae* and human immunodeficiency virus infection leading to increased susceptibility is a serious concern world-wide.⁽⁴⁾

It has been estimated that in India incidence of pneumonia among under-fives is 0.37 episodes/year, resulting in 43 million new cases. Of all pneumonia cases, 7-13% are severe enough to require hospitalization. Pneumonia causes an estimated 408,000 deaths among under-fives contributing to 19% of child mortality in India.⁽⁵⁾

Substantial evidence indicates that common risk factors leading to the development of pneumonia are malnutrition, low birth weight, non-exclusive breast feeding for first 6 months and lack of measles immunization, indoor air pollution and overcrowding. Interventions targeted on most of these risk factors to reduce pneumonia and associated mortality can be effective only in the long-term as they are intimately related to poverty and social-cultural factors.

Thus, currently pneumococcal vaccines seem to be the only public health tool capable of reducing the burden of pneumococcal diseases in developing countries including India and this justifies its inclusion in the National Immunization Program. However, the current cost of the vaccine is prohibitive, being Rs. 1600/dose for 10-valent vaccine and Rs. 3200/dose for the 13-valent

vaccine. This can be overcome for the time being as Global Alliance for Vaccines and Immunization is ready to provide the vaccine at a subsidized price of U\$ 0.15-0.30/dose until 2015. In the meantime, due to bulk requirements the price of the vaccine may come down.

Pneumococcal Vaccines

Pneumococcal vaccines are based on capsular polysaccharide, which is poorly antigenic in children below 2 years of age, the age when there is the highest risk of mortality due to invasive pneumococcal disease (IPD). Pneumococcal conjugate vaccines (PCVs) have been developed to overcome this problem. Depending upon the number of serotypes contained, four types of polysaccharide protein conjugate vaccines were developed, PCV-7, PCV-9, PCV-10 and PCV-13. Currently, only 10 and 13-valent conjugate vaccines are available. Beside these, 23-valent vaccine that is available is non-conjugate vaccine and is effective only in older children and adults.

PCV-7

The 7-valent polysaccharide protein conjugate vaccine (PCV-7) was the earliest to be introduced. It covered 65-80% of serotypes associated with IPD among young children in western countries. It was well-tolerated and had a good safety profile. It also stimulated mucosal immunity, resulting in reduced nasopharyngeal carriage, which in turn helped in developing herd immunity by reducing the transmission of vaccine-type pneumococci. Following primary immunization in infancy, the duration of protection against invasive disease has so far been shown to last at least 2-3 years, but it is expected to last considerably longer.⁽¹⁾ Trials in several developing countries have demonstrated the efficacy of a 3-dose schedule for infants given along with Diphtheria, Pertussis and Tetanus vaccine (DPT) without a subsequent booster dose.

PCV-9

PCV-9 had serotypes 1 and 5 in addition to those in PCV-7. Trials with three dose schedule in South Africa and Gambia showed efficacy of 77-83% against invasive pneumococcal disease due to vaccine serotypes.^(6,7)

PCV-10

PCV-10 has been found to decrease hospitalization for

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pneumonia by 37-50% in Brazil. The Finnish trial has shown effectiveness of 3 + 1 doses of 10-valent vaccine as 100% and that of 2 + 1 doses as 92% against IPD involving vaccine serotypes.⁽⁸⁾

PCV-13

PCV-13 contains polysaccharides of the capsular antigens of *S. pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F. It was introduced for routine administration to infants and children in 2010 in the United States and the United Kingdom. In US, invasive pneumococcal infections decreased by 42% overall and 53% for children <24 months of age in 2011 compared with 2007-2009.⁽⁹⁾

In a study from India, it was observed that PCV-13 had an acceptable safety profile in both infants and toddlers, comparable to that of PCV-7. PCV-13 has immunogenicity similar to PCV-7 in response to the seven common serotypes and generally higher immunogenicity in response to the six additional serotypes.⁽¹⁰⁾

The evidence above suggests that each of the vaccines available currently is effective against the serotypes included in it. Thus with the available choices of vaccines, it becomes extremely important to evaluate the circulating serotypes in a country and then select a suitable vaccine to ensure maximum efficacy and cost-effectiveness.

Serotypes Prevalent in India

In a study published in 1999, the most common serotypes in children under 5 years in *S. pneumoniae* isolates were 6, 1, 19, 14, 4, 5, 45, 12 and 7.⁽¹¹⁾

In a study from Asian countries published in 2011, the serotypes detected were 19F (43.5%), 23F (4.3%), 6B (8.7%), 1 (4.3%), 5 (13.0%), 7F (8.7%), 19A (13.0%), 15 (4.3%).⁽⁴⁾

In a recent study from three hospitals in Delhi published in 2013, out of 108 *S. pneumoniae* isolates tested, serotypes detected were - 19 (26%), 6 (11%), 7 (10%), 1 (9%), 14 (7%), 9 (5%), 33 (4%), 17 (4%), 11 (2%), 3 (2%), 18 (1%), 23 (1%), 12 (1%), 32A (1%), 15B (1%), 22F (1%), 5 (1%), 29 (1%), non-vaccine type E (1%), F (1%) and H (7%).⁽¹²⁾

Although, the available data is patchy and is hospital based, the way forward is to begin with whatever data is available since community based surveillance to study the circulating serotypes representing the entire country will take a long time and monetary resources.

Based on data from the above three studies the most prevalent serotypes currently in India are 6A, 6B, 1, 19F,

Table 1: Comparison of serotypes in India with the serotypes present in the conjugate pneumococcal vaccines

Type of vaccine	Serotypes in the vaccine	Serotypes common among children in India*
7-valent polysaccharide protein conjugate	4, 6B, 9V, 14, 18C, 19F, 23F	6A, 6B, 1, 19A, 19F, 14, 5, 7, 9, 33, and 17
9-valent polysaccharide protein conjugate	1,4, 5, 6B, 9V, 14, 18C, 19F, 23F	6A, 6B, 1, 19A, 19F, 14, 5, 7, 9, 33, and 17
10-valent polysaccharide protein conjugate	1,4, 5, 6B, 7 F, 9V, 14, 18C, 19F, 23F	6A, 6B, 1, 19A, 19F, 14, 5, 7, 9, 33, and 17
13-valent polysaccharide protein conjugate	1,3,4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19 A, 19F, 23F	6A, 6B, 1, 19A, 19F, 14, 5, 7, 9, 33, and 17

*Based on studies in India and Asia,^(4,12,13) Serotypes in bold fonts are not covered in corresponding vaccine

19A, 14, 5, 7, 9V, 33 and 17.

As seen in Table 1, 13-valent vaccine covers two additional serotypes, i.e., 6A and 19A. Of these 19A alone is responsible for 13% of the vaccine type serotypes, whereas separate figures for 6A are not available.^(4,12) Thus, 13-valent PCV should be the vaccine of choice in India, provided its cost gets lower in line with PCV-10. This is evident from a recent study from India, which indicated that 54% of the pneumococcal isolates belonged to PCV-10 and 73% to PCV-13.⁽¹²⁾

The problem of nasopharyngeal colonization by non-vaccine serotypes following the introduction of PCV-7 has not been found to be of serious concern.⁽¹³⁾

To evaluate the effect of introduction of pneumococcal vaccine in the national programme, it will be prudent to institute sentinel surveillance of pneumonia, clinical as well as radiological. The trends obtained when compared with baseline data, will provide a measure of effect of pneumococcal vaccine.

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